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(54) Title: ORAL CARE COMPOSITIONS

(57) Abstract: An oral care composition comprising:(i) an effective amount of a antibacterial seed or pulp extract from the Citrus plant family; the Vitis plant family; and mixtures thereof;(ii) an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; and (iii) a pharmaceutically acceptable carrier.The present invention relates to stable oral care compositions, preferably confectionery compositions, which provide enhanced oral malodour benefits combined with one or more additional oral care benefits. The present invention also relates to the use of such compositions to provide a method of treating or preventing oral malodour.

# ORAL CARE COMPOSITIONS

## Field of the Invention

The present invention relates to oral care compositions, including confectionery compositions, that comprise an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family; an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; and a pharmaceutically acceptable carrier. Preferably this invention relates to oral care compositions comprising grape, and/ or grapefruit seed extract. More preferably this invention relates to the use of these extracts in combination with one or more transition metal cations. This invention also relates to a method of treating or preventing oral malodour. Compositions of the present invention are suitable for use by humans or animals.

## Background of the Invention

Oral malodour or halitosis, which is commonly referred to as bad breath, is the result of volatile sulphur compounds, carboxylic acids and amines building up in the oral cavity. The malodourous compounds are generated primarily through putrefactive action of oral micro organisms on sulphur containing amino acids, peptones or proteins found in the mouth. Such micro-organisms are readily available in saliva and dental plaque and may be derived from proteinaceous food particles trapped between the teeth, in the gingival crevice or adhering to the mucous membranes and the irregular surface of the tongue as well as exfoliated oral epitheleum, food debris and the like. In addition oral malodour may be the result of poor oral hygiene, digestive system problems, disease, diet or a combination of any of these factors. Not only is oral malodour unpleasant but its presence can be indicative of poor oral hygiene and can also be one of the first signs of some more severe underlying problems. This is because the build up of putrid matter which causes malodour can also lead to the formation of plaque, the origin of dental

caries, gingivitis and dental calculus. Regular brushing of teeth can help to minimise oral malodour. However, even regular brushing is not sufficient to remove all of the food and oral bacteria deposits that adhere to the oral surfaces and, in severe cases it is unable to eliminate oral malodour.

To date oral malodour products have been formulated to comprise a wide range of materials that kill the oral bacteria contributing to the oral malodour. Such materials include agents such as triclosan, chlorhexidine, quaternary ammonium salts and camphorated parachlorophenol. However, these materials can be harsh, and can only be dosed in limited daily amounts and as such are not necessarily suitable for use in a product to be used several times a day. In some cases they may also cause undesirable side effects such as staining, altered taste etc.

Metal cations have also been considered for inclusion in oral compositions for treating oral malodour. Disclosures include US 5,833,952 which discloses compositions comprising tin salts, optionally in combination with zinc salts; WO 99/17735 which discloses a metal ion amino acid chelate; US 6,123,925 which discloses a dentifrice comprising ceramic particles in combination with anti-microbial metal ions. However there remain several problems in preparing compositions comprising metal ions for combating oral malodour. These include that the presence of high level of metal cation can often destabilise other elements of the composition, the metal ions become easily chelated to other products and are therefore not efficacious, tightly controlled regulatory limits and the products tend to be highly astringent thus having unacceptable taste profiles. Despite these disadvantages the use of metal cations for combating oral malodour has several benefits. These include that the materials are very cheap, the materials are easy to work with and the metal cations have good recorded efficacy. Thus there remains a desire to continue to work with metal cations to develop a stable, pleasant oral care product able to deliver effective and long lasting malodour benefits.

More recently trends have been directed towards the use so called natural materials, especially extracts, to provide a wide range of benefits in personal care products. Herbal extracts of gold thread and honeysuckle have been reported (JP 57-85319/ US 5,741,138); herbal curry plant extract has been disclosed in JP 10-182,388 for combating halitosis; cranberry extract has been disclosed in WO 96/28135 for is antimicrobial and antibacterial properties; and DE 4,221,103 discloses compositions comprising a wide range of herbal extracts for oral hygiene. Polyphenols have been identified as an important active in a wide range of herbal extracts. Examples of oral care disclosures include WO 01/17494 which discloses dentifrice compositions comprising tea polyphenols; US/PCT/00/11258 which discloses dentifrice compositions comprising polyphenol herbal extracts; and EP 1,013,261 which discloses a spray liquid comprising polyphenol for the masking of halitosis. Whilst the teachings of the prior art are directed towards compositions with limited deodorising or anti-bacterial effects the products themselves have limited activity and are unstable leading to unattractive discolouration over time and further reduction in efficacy. There remains a need for a stable oral care product that is able to deliver effective malodour control benefits.

A new class of compound has recently come to light that has antibacterial benefits. These compounds are the seed and pulp extract from the *Citrus* or *Vitis* plant family. Examples of prior art which disclose *Citrus* pulp and seed extracts include US 5,631,001 which discloses an oral compositions comprising grapefruit pulp and seed extract mixture; JP 6-40,834 which discloses a spray compositions comprising grape fruit seed extract; RO 103,501 which discloses a mouthwash composition comprising alcoholic extracts of citrus plants; JP 4-346,933 discloses an anti-bacterial agent for addition to dentifrice compositions comprising the hexane soluble portion of citrus peel; FR 2,791,893 which discloses oral or topical compositions comprising grapefruit seed extracts; JP 6-40867 which discloses compositions for the prevention and treatment of periodontis comprising citrus fruit seed extract and JP 9-143,084 which discloses an anti-cariogenic agent which comprises grape fruit seed extract. Examples of prior art which disclose *Vitis* seed extract include JP 11-302,142 which discloses food compositions for the prevention of periodontis comprising a polyphenol extract which is optionally obtained from grape; JP

2000-69,945 which discloses a beverage comprising grape extract; and US 5,891,465 which discloses nutritional supplements comprising a wide range of lipid encapsulated materials for administration as a liquid or aerosol spray wherein the preferred supplement comprises grape extract. Whilst the teachings of the prior art discloses how to formulate simple compositions, including simple oral care compositions comprising the seed or pulp antibacterial extracts there remains a need to prepare a product which is able to not only deliver the extract but also to combine this with a further oral care active such that the final product has multiple activity and can deliver more holistic oral care benefits. In addition the oral malodour benefits of such extracts have not previously been discussed. Furthermore it is likely that such extracts, in common with other similar plant extracts, are unstable in complex formulations. As such there remains a need to stabilise compositions comprising such materials.

As well as improving the oral malodour benefits of oral care products there is also an industry move to develop portable oral care products. This enables consumers to use such products several times a day, especially immediately after eating and throughout the day which will prevent the build up of food deposits which can enhance activity of the plaque forming microbes and the return of oral malodour. Such products are also useful for pets and children where it is not always easy or possible to regularly brush the teeth.

Confectionery compositions which are popular with both children and adults alike and which are retained in the oral cavity for substantial periods of time during consumption, would seem to make an ideal product form for a portable oral care product. Furthermore chewing gums have many benefits as a portable oral care form since they remain within the oral cavity for significant periods of time, typically 20 minutes or longer. The art of the development and manufacture of a wide range of confectionery compositions is well known. However, the high sugar content of such confectionery compositions has been recognised as a contributory factor in poor dental health. Developments have been made to produce "sugar free", or non cariogenic, confectionery which retain their organoleptic properties but which do not contribute to the formation of dental plaque. More recently

research has turned to developing confectionery compositions, particularly "sugar free" confectionery compositions, particularly chewing gum compositions, which comprise one or more oral care agents. One such example is WO 99/44436 which discloses coated chewing gum compositions which comprise materials with known oral care benefits. There exists a need therefore for a wide range of confectionery compositions which have oral malodour benefits. In addition there is a need for such compositions to be able to deliver a wide range of oral care benefits including more effective oral malodour control benefits thus providing a composition which is able to deliver a wide range of oral care benefits.

Turning to the confectionery art there are isolated disclosures of compositions comprising natural extracts. These include JP 2000-189,060 which discloses gelatine compositions comprising polyphenol for the removal of teeth staining; JP 10-257856 which discloses a chewing gum composition comprising polyphenol for the prevention of influenza and WO 99/44440 which discloses a food composition comprising tea polyphenol for the prevention of periodontis. Again whilst the teachings of the prior art are directed towards the development of a confectionery composition comprising some natural extracts, *Citrus* and or *Vitis* have not been disclosed in confectionery compositions to date. There remains a need to develop a confectionery composition for effective treatment of oral malodour. In addition there remains a need to develop confectionery compositions which not only have oral malodour benefits but which also comprise one or more further oral hygiene benefits.

Surprisingly, it has now been found that, when an oral care product is prepared comprising an effective amount of a seed or pulp extract from the *Citrus* or *Vitis* plant family and one or more further oral care actives, a composition is obtained which not delivers effective oral care benefits including oral malodour benefits. Furthermore, by preferably formulating the product with less than about 10% water the compositions and the extracts remain stable resulting in compositions that do not degrade or discolour over

time. Finally by preferably preparing the product in stable confectionery forms, portable oral care, which provides comparable benefits to frequent brushing, has been developed.

While not wishing to be bound by theory it is believed that when an oral care composition is formulated comprising a seed or pulp antibacterial extract from *Citrus* or *Vitis* plant family that the active components interact with the oral microbes that perpetuate the malodour altering their cell membrane and inhibiting their enzymatic activity. . It is believed that they act by disorganising the cytoplasmic membrane thereby preventing uptake of amino acids. It is also believed that the extract disorganises the cell membrane by inactivation of cellular respiration leading to the formation of "pores" in the membrane itself. Low molecular weight cellular contents are then able to leak out through the cytoplasmic membrane. Over time the microbe is deactivated and dies. It is believed that the synergisitic activity of each of the many components that make up the extract act together to provide an improved antibacterial and antimicrobial effect.

When used in addition with a further oral care active both basic and complex synergistic effects can be noted. For example, if the extract is used in addition with a desensitising agent eg potassium nitrate, the overall oral benefits experienced are those of both agents singly eg malodour reduction and desensitisation. This is an example of basic synergy. However, more complex synergistic benefits can also be noted. For example if extract is used in conjunction with another anti-plaque agent the action of the extract in disrupting the cell membrane of the bacteria can make the bacteria themselves more susceptible to the further anti-plaque agent thus resulting in a greater plaque reduction than would be seen with either active alone.

Surprisingly, it has also been found that there are particularly interesting synergistic effects found when the *Citrus* or *Vitis* seed or pulp extract is combined with a metal cation with oral malodour activity. The metal cations when used alone are thought to exhibit their oral malodour effects by complexing with the volatile malodour producing compounds to provide a long lasting bad breath reduction. In addition it is also believed

that the metal cations interact with the oral microbes. They are likely taken into the cell cytoplasm by active transport across the cell membrane. Once inside the cell the metal cations can act to inhibit the cell activity and eventually kill the organisms thus further reducing oral malodour and plaque. These effects can be further enhanced by the use of a combination of different metal cations. This can also have the benefit of enabling the low regulatory levels for any single metal cation to be overcome whilst still ensuring an efficacious product. Finally, if the metal cations are used in a low level water composition the use of a variety of salts with different solubility profiles can lead to a staggered and controlled release of the metal cations over time.

By using a combination of the antibacterial extract with a metal cation further surprising benefits are obtained. It is believed that the two materials work together synergistically to provide an enhanced oral malodour effect than would be achieved by using the materials individually. Whilst not wishing to be bound by theory it is believed that this effect is caused by the action of the materials on the microbes in the oral cavity which help to perpetuate malodour. It is believed that the extracts disrupt the cell membrane thus increasing their porosity. This enables a greater number of the metal cations to pass into the cell cytoplasm thus enhancing the disruptive effect. This results in a greater reduction in the organisms than would be seen by use of either material alone. Again it is believed that this activity is further enhanced if a mixture of more than one metal cation is used. Furthermore by formulating these actives into a wide range of oral care compositions, particularly confectionery compositions, designed to be held in the oral cavity for substantial periods of time the action of the actives is further enhanced.

It is an object of the present invention to provide a wide range of oral compositions with oral malodour control benefits, suitable for use by adults, children and pets. It is a further object of this invention to prepare an oral care composition which is not only capable of providing superior oral malodour benefits but also capable of providing a range of other oral care benefits. It is also an object of this invention to maximise the synergistic effects gained by using oral malodour control agents with different mechanisms of action in the

same composition. Finally it is an object of this invention to stably formulate a wide range of product forms including confectionery with these benefits. These and other objects of the present invention will become readily apparent from the detailed description that follows.

## Summary of the Invention

According to a first aspect the present invention relates to an oral care composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family and mixtures thereof;

(ii) an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; and

(iii) a pharmaceutically acceptable carrier.

According to a second aspect the present invention relates to an oral composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family and mixtures thereof;

(ii) a metal cation selected from the metals of groups 5, 6, 7, 8, 9, 10, 11, 12, 14, 16 of the periodic table and mixtures thereof;

(iii) a pharmaceutically acceptable carrier.

According to a third aspect the present invention relates to a method of preventing or treating halitosis comprising applying to the oral cavity a composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family and mixtures thereof;

(ii) a metal cation selected from the metals of groups 5, 6, 7, 8, 9, 10, 11, 12, 14, 16 of the periodic table and mixtures thereof;

(iii) a pharmaceutically acceptable carrier.

and retaining said composition in the oral cavity for at least 5 seconds, preferably at least 10 seconds, more preferably at least 15 seconds and most preferably at least 30 seconds.

## Detailed Description of the Invention

All percentages and ratios used herein are by weight of the total composition and all measurements made are at 25°C, unless otherwise designated.

All publications cited herein are hereby incorporated by reference in their entirety, unless otherwise indicated.

The term "safe and effective amount" as used herein means an amount of a compound, component, or composition sufficient to significantly induce a positive benefit, but low enough to avoid serious side effects, i.e. to provide a reasonable benefit to risk ratio, within the scope of sound medical judgement.

The term "orally active" as used herein means a material that provides either a cosmetic, prophylactic or therapeutic benefit within the oral cavity.

The term "oral composition" as used herein means the total composition that is delivered to the oral surfaces. The composition is further defined as a product which, during the normal course of usage, is not, the purposes of systemic administration of particular therapeutic agents, intentionally swallowed but is rather retained in the oral cavity for a time sufficient to contact substantially all of the dental surfaces and / or oral tissues for the purposes of oral activity. Examples of such compositions include, but are not limited to, toothpaste, dentifrice, mouthwash or mouth rinses, topical oral gels, denture cleanser, mouth spray, dental floss, confectionery including chewing gum and lozenge, and the like. It is preferred that the compositions of the present invention are toothpaste or dentifrice compositions, mouth wash or mouth rinse compositions or confectionery compositions. It is even more preferred that the compositions of the present invention are confectionery compositions.

The term "dentifrice" as used herein means paste, gel, or liquid formulations unless otherwise specified. The dentifrice composition can be in any desired form such as deep striped, surface striped, multi-layered, having the gel surrounding the paste, or any

combination thereof. Alternatively the oral composition may be dual phase dispensed from a separated compartment dispenser.

The term "confectionery" as defined herein means a solid, gum, gum-like, or glassy composition optionally having a liquid centre filling and/or optionally coated which comprises greater than about 25% sugar or sugar alcohol. Such compositions usually have a sweet taste. Examples of confectionery products include, but are not limited to, breath mints, low boiled candy, chewing gum, hard boiled candy, coated candy, lozenges, oral pasta, pressed mints, throat drops and the like.

The term "chewing gum" as defined herein means a confectionery composition which is suitable for chewing and which comprises 2% or greater, by weight of the composition, of elastomer.

The term "gum base" as defined herein means a material or mixture of materials which is used in confectionery composition but which comprises a non-digestible elastomer, plastic or resin.

The term "elastomer" as defined herein means a non-digestible polymeric material, or mixture of materials, such as the materials typically used in chewing gum compositions.

The term "crunchy" as defined herein means that the product has a texture such that has a firm and slightly gritty texture and which produces a slight cracking noise upon consumption. It is preferred that the compositions have a texture of granulated sugar.

Active and other ingredients useful herein may be categorised or described herein by their cosmetic and/or therapeutic benefit or their postulated mode of action. However, it is to be understood that the active and other ingredients useful herein can in some instances provide more than one therapeutic and/or cosmetic benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit an ingredient to the particularly stated application or applications listed.

The elements of the compositions and methods of the present invention are described in more detail below.

***Antibacterial Extracts***

Compositions of the present invention comprise an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family. The extracts are preferably obtained from the plant group consisting of bergamot or bitter orange (*Citrus aurantiums*); grapefruit (*Citrus Grandis, Citrus Paradisi*); orange (*Citrus Sinesis*); lemon (*Citrus medica limonium, Citrus limon*); lime (*Citrus aurantifolia*); tangerine (*Citrus reticulata*); mandarin (*Citrus reticulata*); Satsuma (*Citrus reticulata*); clementine (*Citrus reticulata*); citron (*Citrus medica*); shaddock (*Citrus Maxima*); grape (*Vitis vinifera*) and mixtures thereof; preferably selected from the group consisting of bergamot (*Citrus Aurantiums*); grapefruit (*Citrus Grandis, Citrus Paradisi*); orange (*Citrus Sinesis*); lemon (*Citrus medica limonium*); lime (*Citrus aurantifolia*); grape (*Vitis vinifera*); and mixtures thereof, more preferably selected from grapefruit (*Citrus Grandis, Citrus Paradisi*); grape (*Vitis vinifera*) and mixtures thereof. Highly preferred are the commercially available grapefruit seed extract Citracidal from Bio/Chem, Lakeport Claifornia USA; Citroseed Liquid available from Laboratorio Centroflora Ltd, Sao Paulo, Brazil; Grapefruit seed extract from Goerlich Pharma GmbH, Edling, Germany; Grape seed extract from Vinyals Botanicals, Barcelona Spain; Grape seed extract available from Dragoco Ltd, Weybridge, Surrey UK and mixtures thereof.

The antibacterial extracts for use herein are extracted from the seed or pulp or white membrane or pericarp of the fruit or mixtures thereof; preferably from the seed or pulp or mixtures thereof and more preferably from the seed.

Such extracts comprise a wide variety of biologically active materials. These include many types of polyphenols, anthocyanins, flavanols, hydrolysable tannins, alkaloids, lipids, carbohydrates, simple sugars, protein and amino acids, alcohols and organic acids as well as. It is believed that the active component of the extracts is the polyphenol materials. As used herein the term "polyphenol" is defined to mean a chemical compound which comprises more than one phenol group, preferably greater than two phenol groups and more preferably greater than three phenol groups. As used herein the term "phenol group" is defined to mean an aromatic six member carbon ring to which is bonded at least one alcohol group. Extracts suitable for use in compositions of the

present invention preferably comprise greater than about 1%, preferably greater than about 5%, more preferably greater than about 10% and most preferably greater than about 15%, by weight of the extract, polyphenol material. The extract may comprise up to 100% polyphenol material. The preferred and highly preferred extracts are chosen because they comprise particular types of polyphenols or higher levels of polyphenol materials. Grapefruit seed extract specifically comprises the polyphenols quertcitin, quercetin glycoside, helperidin, campherol glycoside, apigenin, rutinoside, hepamothoxyflavone, dihydrocampherol glycoside which are stabilised by being converted to ammonium salts in the extract mixture. It also comprises the flavanoids narigin, isoacuranetin, neohesperidin, hesperidin, poncirin, nobiletin and tangeretin. Grape seed extract comprises the polyphenols from the chemical class of flavonoids. These can be further broken down into flavnaol, proanthocynidins, flavanones and flavononls (from grape skin), anthocyanins, anthocyanidinds, and anthocyanosides.

Many extracts of this type also comprise ascorbic acid. It is preferred that extracts for use in the present invention comprise less than about 15%, preferably less than about 12% and more preferably less than about 10%, by weight of the extract, of ascorbic acid.

The extracts deliver oral health benefits due to their ability to inhibit the growth of certain bacteria eg *S. mutans, P. ginigvilis* and *F. nuclearum* in both low and high concentrations. These bacteria are commonly acknowledged to be among the main sources of oral diseases and breath malodour. The extract is considered to have anti-bacterial efficacy when it displays a minimum inhibitory concentration (MIC) of less than 20,000ppm, preferably less than 10,000ppm, and more preferably less than 5,000ppm vs one or more of the above bacteria. Furthermore no proliferation of said bacteria should occur in the presence of greater than or equal to 20,000ppm of extract under conditions suitable for growth of said bacteria. The MIC level is measured by standard techniques that are well known to one skilled in the art.

The extracts for use in the present invention can be obtained from the plant material by a variety of different methods. These include pressing, extraction, distillation, and mixtures thereof. It is preferred that extracts used herein are obtained by solvent extraction, including super critical fluid extraction, preferably solvent extraction using solvents

selected from the group consisting of alcohols, water, acetone, ethyl acetate, glycerol, diethyl ether, propylene glycol and mixtures thereof, preferably the solvent is selected from the group consisting of water, alcohols, glycerol, propylene glycol and mixtures thereof.

The extracts are safe and suitable for use for humans and pets. It is preferred that compositions of the present invention comprise from about 0.0001% to about 30%, preferably from about 0.001% to about 15%, more preferably from about 0.01% to about 10%, even more preferably from about 0.1% to about 5% and most preferably from about 0.25% to about 3%, by weight of the composition, of antibacterial seed or pulp extract.

When using such extracts in oral compositions it is important to ensure that the upper limit of the extract level is controlled such that the extract does not cause any undesirable damage to the oral cavity, particularly to the tooth enamel. This is particularly important when using extracts derived from the *Citrus* family, and more especially when using grapefruit seed extract.

Compositions of the present invention may optionally comprise zinc phytate in combination with natural extracts comprising polyphenols. The zinc phytate is believed to enhance the polyphenol breath protection efficacy and increase the stability of the polyphenol extract. It may also independently product breath protection, anti-plaque protection and anti-bacterial efficacy. Compositions of the present invention preferably comprise from about 0.1% to about 10%, more preferably from about 0.5% to about 5% and most preferably from about 1% to about 3%, by weight of the composition, of zinc phytate.

Extracts for use in the present invention can optionally be encapsulated. Such encapsulation can have several benefits including stabilising the polyphenols in formula, and can provide for controlled release mechanisms. Encapsulation can be in the form of vesicles or lipsomes with unilamellar, bilamellar or multilamellar structures. Such encapsulates can be formed by the use of emulsifying agents, fatty acids eg lecithin. Encapsulation can also be made using compounds that complex the polyphenols such as cyclodextrin. Similarly polyphenols can be adsorbed within inorganic structures such as silica shell, zeolites.

*Oral Care Active*

Compositions of the present invention comprise an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; preferably from the group consisting of anti-calculus agents including polyphosphates, pyrophosphates, phosphonates and mixtures thereof; the group of anti-plaque agents comprising a fluoride ion source, xylitol and mixtures thereof; the group of desensitising agents, preferably potassium nitrate; and mixtures thereof; oral malodour control agents selected from metal salts, natural extracts and mixtures thereof; more preferably the oral care active is an anti-calculus agent; more preferably the oral care active is polyphosphate. It is not intended that the actives listed in groups below are mutually exclusive and a single active may be included in compositions of the present invention to have several effects. It is highly preferred that the oral care active is a solid.

Compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1% to about 15%, even more preferably from about 0.25% to about 10%, and most preferably from about 0.5% to about 7%, by weight, of oral care active.

Anti-calculus Agents: Anti-calculus agents known for use in dental care products include phosphate, pyrophosphate, polyphosphate, phosphonate, polyphosphonate and mixtures thereof. **Pyrophosphates** are among the best known for use in dental care products. The pyrophosphate salts useful in the present compositions include the dialkali metal pyrophosphate salts, tetra-alkali metal pyrophosphate salts and mixtures thereof in their unhydrated as well as hydrated forms are the preferred species. Disodium dihydrogen pyrophosphate ($Na_2H_2P_2O_7$), tetrasodium pyrophosphate ($Na_4P_2O_7$), and tetrapotassium pyrophosphate ($K_4P_2O_7$) and mixtures thereof.

**Polyphosphates** are the highly preferred anti-calculus agents. Compositions of the present invention preferably comprise greater than about 1%, preferably from about 1.5% to about 50%, more preferably from about 2% to about 15%, even more preferably from about 3% to about 12%, and most preferably from about 5% to about 10%, by weight, of polyphosphate salt. Polyphosphate is a widely used term which relates to phosphate

anions which have been polymerised by dehydration to form a polymer of the phosphate anion. The polyphosphates can exist as linear or cyclic materials or mixtures thereof. It is preferred that the polyphosphates are linear materials comprising only low levels of cyclic materials. Polyphosphates are also characterised by the average anion chain length of the polymer. For the purposes of this invention the polyphosphates referred to are those with an average anion chain length of 3 or greater. It is preferred that the polyphosphates have an average anion chain length of from about 3 to about 40, preferably of from about 6 to about 30; more preferably of from about 10 to about 25 and even more preferably of from about 18 to about 25, and mixtures thereof. Furthermore polyphosphates exist as salts. It is preferred that the polyphosphate is an alkali metal salt or mixtures thereof, preferably a sodium or potassium salt or mixtures thereof and more preferably a sodium salt. Polyphosphates with an average anion chain length of greater than four usually occur as glassy materials. As defined herein a "glassy" material is one which is amorphous. Preferred in this invention are the linear "glassy" polyphosphates having the formula:

$$XO(XPO_3)_nX$$

wherein X is sodium, potassium, or hydrogen and n averages greater than or equal to 6 or mixtures thereof. Such polyphosphates are manufactured by FMC Corporation and are commercially known as Sodaphos (n≈6), Hexaphos (n≈13), and Glass H (n≈21). Hexaphos and Glass H are preferred with Glass H being the most preferred polyphosphate. These polyphosphates may be used alone or in combination. A broad range of phosphates and their sources are described in Kirk & Othermer, *Encyclopedia of Chemical Technology*, Fourth Edition, Volume 18, Wiley-Interscience Publishers (1996), incorporated herein by reference in its entirety, including all references incorporated into Kirk & Othermer. Polyphosphates and pyrophosphate salts have been found to have a synergistic effect when combined in a composition with an anti-microbial extract. It is believed that this is as a result of their mechanisms of action. The phosphate salts act in part to prevent the attachment of plaque to the teeth. At the same time the extract is working to reduce the level of plaque in the mouth. It is believed that the extract is able to be more effective when the oral microbes are not attached to the surface of the teeth.

Thus, by combining these two materials surprisingly better effects are achieved than would be achieved by using either alone.

**Additional anti-calculus agents** include polyacrylates and other polycarboxylates such as those disclosed in US Patent No 3,429,963 issued to Shedlovsky on February 25, 1969 and US Patent No 4,304,766 issued to Chang on December 8, 1981; and US Patent No 4,661,341 issued to Benedict and Sunberg on April 28, 1987; polyepoxysuccinates such as those disclosed in US Patent No 4,846,650 issued to Bendict, Bush and Sunberg on July 11, 1989; ethylenediaminetetraacetic acid as disclosed in British Patent No 490,384 date February 15, 1937; nitrilotriacetic acid and related compounds as disclosed in US Patent No 3,678,154 issued to Widder and Briner on July 18, 1972; polyphosphonates as disclosed in US Patent No 3,737,533 issued to Francis on June 5, 1973; US Patent No 3,988,443 issued to Ploger, Schmidt-Dunker and Gloxhuber on October 26, 1976 and US Patent No 4,877,603 issued to Degenhardt and Kozikowski on October 31, 1989.

Anti-plaque Agents: Anti-plaque agents include anti-plaque agents and flouride ion sources. **Anti-plaque agents** are any substances which inhibit the accumulation of bacterial deposits on the surfaces of the oral cavity. Examples include xylitol and other anti-microbial agents. The inhibition effects of the xylitol on oral microbes is able to have better effect when used in conjunction with an extract since the extract is also acting to disable the microbes.

Fluoride Ion source: Application of **fluoride ions** to dental enamel serves to protect teeth against decay. A wide variety of fluoride ion yielding materials can be employed as sources of soluble fluoride in the present compositions. Examples of suitable fluoride ion yielding materials are found in US Patent No 3,535,421, October 20, 1970 issued to Briner et al and US Patent No 3,678,154 July 18, 1972 issued to Widder et al. Preferred fluoride ion sources for use herein include sodium fluoride, potassium fluoride, stannous fluoride, ammonium fluoride and mixtures thereof. Sodium fluoride is particularly preferred. Preferably the present composition provide from about 50ppm to about 10,000ppm, more preferably from about 100ppm to about 3000ppm of fluoride ions. Again it is believed that when used in conjunction with one of the natural extracts claimed herein the fluoride ions are able to have better effect since there has been a

reduction in plaque and microbe activity in the oral cavity due to the anti-bacterial effect of the extract.

Desensitising Agents: Desensitising agents, or anti-pain agents, can also be present in the oral care compositions or substances of the present invention. Such agents may include, but are not limited to, strontium chloride, potassium nitrate, natural herbs such as gall nut, Asarum, Cubebin, Galanga, scutellaria, Liangmianzhen, Baizhi, etc. Analgesics, including low levels of non-steroidal anti-inflammatory agents, such as ketorolac, flurbinprofen, ibuprofen, naproxen, indomethacin, aspirin, ketoprofen, piroxicam and meclofenamic acid, may also be used as desensitising agents.

Oral Maldour Control Agents: Oral malodour control agents include a wide variety of materials. The most commonly used are **antimicrobial agents** can also be present in the oral care compositions or substances of the present invention. Such agents may include, but are not limited to, 5-chloro-2-(2, 4-dichlorophenoxy)-phenol, commonly referred to as triclosan, and described in the Merck Index, 11th Edition, (1989), pp1529 (entry no 9573) in US Patent No 3,506,720, and in European Patent Application No 0,251,591 of Beecham Group, Plc, published January 7th, 1988; phthalic acid and its salts including, but not limited to those disclosed in US Patent 4,994,262 published February 19th, 1991, preferably magnesium mono-potassium phthalate, chlorhexidine (Merck Index, no 2090); alexidine (Merck Index, no 222); hexetidine (Merck Index, no 4624); sanguinarine (Merck Index, no 8320); benzalkonium chloride (Merck Index, no 1066); salicylanilide (Merck Index, no 8299); domiphen bromide (Merck Index, no 3411); cetylpyridinium chloride (CPC) (Merck Index, no 2024); tetradecylpyridinium chloride (TPC); N-tetradecyl-4-ethylpyridinium chloride (TDEPC); octenifine; delmopinol; octapinol; and other piperidine derivatives; nicin preparations; zinc/stannous ion agents; antibiotics such as augmentin, amoxicilline, tetracycline, doxycycline, minocycline, and metronidazole; and analogues and salts of the above; methyl salicyclate; and mixtures of all of the above.

**Metal Cations** are also commonly used as anti-bacterial agents. The metal cation is selected from the metals of group 5 (V, Nb, Ta); group 6 (Cr, Mo, W); group 7 (Mn, Tc, Re); group 8 (Fe, Ru, Os); group 9 (Co, Rh, Ir); group 10 (Ni, Pd, Pt); group 11 (Cu, Ag, Au); group 12 (Zn, Cd, Hg); group 14 (Ge, Sn, Pb); group 16 (Se, Te, PO); and mixtures

thereof. Preferably the metal cation is selected from any monovalent or divalent cation selected from the group consisting of zinc, manganese, copper, iron, cobalt, silver, selenium, tin and vanadium; preferably from the group consisting of zinc, manganese, copper, iron, silver, and tin; more preferably from the group consisting of zinc, copper, silver and tin and most preferably from the group consisting of zinc and tin.

A wide variety of metal cation salts are useful in the present invention. These include so called "water-insoluble salts" which have a solubility of less than about 0.5g per 100ml at 25°C and "water soluble salts" which have a solubility of greater than or equal to about 0.5g per 100ml at 25°C. It is also possible to use mixtures of these salts. Such mixtures can have several advantages in the compositions of the present invention since they are likely to have different complexing properties with the polyphosphate anions. In addition they have different release rates in the saliva and can therefore act to provide controlled release profiles. Examples of salts that are suitable for use herein include acetate, ammonium sulphate, bromide, chloride, chromate, citrate, dithionate, fluorosilicate, tartrate, fluoride, formate, iodide, nitrate, phenol sulphate, salicyclate, sulphate, gluconate, succinate, glycerophosphate, lactate and mixtures thereof; preferred are acetate, bromide, chloride, citrate, dithionate, tartrate, fluoride, formate, iodide, nitrate, sulphate, gluconate, succinate, lactate and mixtures thereof; and more preferred are acetate, chloride, citrate, sulphate, gluconate, succinate, lactate and mixtures thereof. If stannous chloride is used it may be advantageous to premix the stannous chloride with sodium gluconate prior to incorporating the salt in the composition since this can help to stabilise the stannous ions.

When a metal cation is incorporated into compositions of the present invention, which additionally comprise polyphosphate, the additional benefit of reducing the astringency of the metal cations within the composition is obtained thus improving the taste. In order to maximise this benefit it is preferred that the molar ratio of polyphosphate anion to the total level of orally active metal cation should be in the range of from about 10:1 to about 1:1, preferably from about 5:1 to about 1:1, preferably from about 3:1 to about 1:1. As used herein the term "polyphosphate anion" refers to a single anion regardless of chain length. The level of polyphosphate anion should be calculated by assuming that all of the polyphosphate material has the chain length of the average anion chain length of the

material as quoted by the manufacturer. Compositions of the present invention comprise greater than 10ppm, preferably greater than 15ppm, more preferably greater than 20ppm, even more preferably greater than 25ppm of the orally active metal cation. Compositions of the present invention preferably comprise from about 0.001% to about 5%, preferably from about 0.01% to about 2%, more preferably from about 0.1% to about 1% and most preferably from about 0.1% to about 0.5%, by weight of the composition, of metal salt comprising the orally active metal cation. The strong synergistic relationship achieved by combining metal cations and natural extracts in the same composition has already beeen described in the background section.

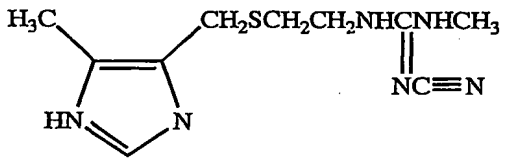
A further group of **natural extracts** which are useful for their oral malodour control benefits include extracts obtained from the tea, honey suckle, gold thread, magnolia plants or mixtures thereof. Extracts suitable for use in the present invention can be obtained from any part of the plant including the leaf, stem, bark, pulp, seed, flesh, juice, root and mixtures thereof. It is preferred that compositions of the present invention comprise from about 0.1% to about 5% and preferably from about 0.25% to about 3%, by weight of the composition, of antibacterial seed or pulp extract.

The following **essential oils** are also known to have anti-microbial activity and are therefore optionally used in compositions of the present invention. These oils include thymol, geraniol, carvacrol, hinokitiol, eucalyptol, catechol (particularly 4-allyl catechol) and mixtures thereof.

Another class of oral malodour control agents include **absorbents**. These are used to absorb, adsorb, bind or otherwise complex the volatile oral malodour materials. Examples of such agents include talc, mushroom extract, zeolite, cyclodextrin, silica shell and mixtures thereof. Such materials are preferably used at a level of from about 0.5% to about 10%, preferably from about 1% to about 5%, by weight of the composition.

H-2 Antagonists: Histamine-2 (H-2) receptor antagonist compounds (H-2 antagonists) may be used in the oral care compositions of the present invention. As used herein, selective H-2 antagonists are compounds that block H-2 receptors, but do not have meaningful activity in blocking histamine -1 (H-1) receptors. Selective H-2 antagonists include those disclosed in US Patents 5,294,433 and 5,364,616 Singer et al., issued 15th

March 1994 and 15th November 1994 respectively and assigned to Procter & Gamble, wherein the selective H-2 antagonist is selected from the group consisting of cimetidine, etintidine, ranitidine, ICIA-5165, tiotidine, ORF-17578, lupititidine, donetidine, famotidine, roxatidiein, pifatidine, lamtidine, BL-6548, BMY-25271, zaltidine, nizatidine, mifentidine, BMY-52368, SKF-94482, BL-6341A, ICI-162846, ramixotidine, Wy-45727, SR-58042, BMY-25405, loxtidine, DA-4634, bisfentidine, sufotidine, ebrotidine, HE-30-256, D-16637, FRG-8813, FRG-8701, impromidine, L-643728 and HB-408.4. Particularly preferred is cimetidien (SKF-92334), N-cyano-N'-methyl-N''-(2-(((5-methyl-1H-imidazol-4- yl)methyl)thio)ethyl)guanidine:




Cimetidine is also disclosed in the Merck Indes, 11th editions (1989), p354 (entry no 2279), and Physicians' Desk Reference, 46th edition (1992), p2228. Related preferred H-2 antagonists include burimamide and metiamide. Again it is believed that an enhanced synergistic effecti is achieved by using the natural extracts disclosed herein in combination with the H2 antagonists. This is because whilst the antagonist acts to reduce inflammation the extract is able to have an anti-bacterial effect in reducing the level of infection. Thus by use of the two together more effective reduction in disease is achieved than by using either alone.

***Carrier Materials***

Compositions of the present invention comprise a carrier material into which other ingredients are solubilised, dispersed or otherwise mixed. Depending upon the type of composition in question the carrier material can differ. For example mouth wash compositions commonly have a carrier material which comprises from about 20:1 to about 2:1 aqueous alcoholic matrix; dentifrice compositions usually comprise an aqueous matrix system; denture cleansers which are usually hard pressed tablets, dental floss where the carrier is a fibre or paper material and confectionery compositions wherein the carrier material is a sweetener matrix. The preferred compositions of the present

invention are dentifrice, mouthwash and confectionery compositions including chewing gum. It is preferred that non-confectionery compositions of the present invention are single phase compositions by which is meant that the whole composition is stably stored within a single container. The most important elements of the carrier systems for these products are discussed below.

Water

Water used in the preparation of commercially suitable compositions should preferably be of low ion content and free of organic impurities. The amount of water in a composition should be considered to be not only that added as free water, but also water which is introduced with other materials, such as with sorbitol, silica, surfactant solutions and or colour solutions.

Compositions of the present invention can comprise water from about 0.1% to about 99%, preferably from about 0.5% to about 50%, by weight of the composition. It is highly preferred that compositions of the present invention comprises less than about 10%, preferably less than about 8%, more preferably less than about 5%, even more preferably less than about 3%, and most preferably less than about 2%, by weight of the composition, water. The low levels of water are required in order to ensure that the polyphenol components of the plant extracts are not oxidised and, if included, any long chain polyphosphates are not hydrolysed in the final composition.

Confectionery Carrier Material

Compositions of the present invention are confectionery compositions including chewing gum. Suitable physical forms include sticks, dragees, chicklets, and batons. Although the exact ingredients for each product form will vary from product to product, the specific techniques will be known by one skilled in the art. However there are some general ingredients which are common to all product forms and these are discussed in more detail below. Preferred product forms are pressed tablets, low boiled candy, hard boiled candy

and chewing gum which are readily formulated with less than about 10%, by weight of the composition, water.

Confectionery compositions of the present invention comprise a carrier material. The carrier materials vary depending on the type of confectionery used and would be well known to one skilled in the art. The carrier material can be chosen from chewable or non chewble materials. It is referred that the compositions comprise at least 10% chewable material. The chewable material can be selected from gums including agar agar gum, gelatine etc; low boiled sugar candy base and gum base materials. It is preferred that the carrier material for compositions of the present invention are not in the form of a whippable or aerated emulsion. Hard and low boiled candy carrier, pressed tablets and the like usually comprise greater than about 70% bulk sweetener including suitable sugar and sugar syrups including cariogenic and non-cariogenic materials. Low boiled candies can also comprise butter to form chewable toffee. For jelly and gum drop compositions the carrier comprises greater than about 25% bulk sweetener and additionally comprise gums including gum arabic, gelatine, agar agar powder and the like.

Compositions of the present invention are preferably in the form of a chewing gum. As such it is preferred that the compositions comprise greater than about 10%, preferably greater than about 15%, more preferably greater than about 20% and most preferably greater than about 25%, up top 75%, by weight of the composition, of gum base. The gum base comprises a carrier material, or mixture of carrier materials, selected from elastomers, resins or waxes. The gum base carrier materials are water insoluble materials which are typically not released in the mouth. Such materials include:

(i) Elastomers and Elastomer Solvents

Compositions of the present invention preferably comprise an elastomer, or mixture of several different elastomers. Elastomeric materials are generally known in the art but illustrative examples include styrene-butadiene rubber (SBR); synthetic gums; polyisobutylene and isobutylene-isoprene copolymers; natural gums; chicle; natural rubber; jelutong; balata; guttapercha; lechi caspi; sorva; and mixtures thereof. Compositions of the present invention preferably comprise from about 2% to about 30%, more preferably from about 5% to about 25%, by weight, of elastomer. These levels are determined by the desired final texture of the chewing gum since when the total level of

elastomer is below about 2% the base composition lacks elasticity, chewing texture, and cohesiveness whereas at levels above about 30% the formulation is hard, rubbery and maintains a tight chew.

Elastomer solvents are also preferably present in compositions of the present invention since they aid softening of the elastomer component. Preferred examples of elastomer solvents for use herein include the pentaerythritol ester of partially hydrogenated wood rosin, pentaerythritol ester of wood rosin, glycerol ester of partially dimerized rosin, glycerol ester of polymerised rosin, glycerol ester of tall oil, wood or gum rosin, glycerol ester of partially hydrogenated rosin, methyl ester of partially hydrogenated rosin, and mixtures thereof. Compositions of the present invention preferably comprise from about 2% to about 50%, more preferably from about 10% to about 35%, by weight, of elastomer solvent.

(ii) Resins and Waxes

Resins are an optional, but desirable, ingredient of chewing gum compositions herein. They serve to plasticise the gum base. Suitable resins include polyvinyl acetate (PVA); terpene resins, including polyterpene and polymers of alpha-pinene or beta-pinene; and mixtures thereof. Such compositions preferably comprise from about 3% to about 25%, preferably from about 5% to about 20%, by weight, of resin.

The chewing gum compositions may also include one or more waxes. Suitable waxes include paraffin wax; microcrystalline wax; Fischer-Tropsch paraffin; natural waxes such as candellilla, carnauba and beeswax; polyolefin waxes such as polyethylene wax; and mixtures thereof. Compositions comprise up to about 25%, preferably from about 5% to about 20%, by weight, of wax.

Confectionery compositions of the present invention can be centre filled. Such products preferably comprise from about 60% to about 95%, more preferably from about 75% to about 85% of an edible shell and from about 5% to about 40%, preferably from about 15% to bout 25%, by weight of the composition, of an edible filling. It is possible that centre filled confectionery composition can comprise an oral care active in the edible shell and or a different oral care active, or mixture of actives, in the edible filling. In

addition the composition can comprise different flavouring agents in the shell and the filling.

Compositions of the present invention may comprise one or more crunchy solid particles dispersed throughout the carrier material. The crunchy preferably particle has a minimum particle size such that the particles are retained by a 0.1mm mesh, preferably a 0.112mm mesh, more preferably a 0.16mm mesh, even more preferably a 0.18mm mesh and most preferably a 0.2mm mesh wherein the meshes are selected from the DIN 4188 mesh series. Furthermore the particle preferably has a maximum particle size such that it passes through a 2mm mesh, preferably a 1mm mesh, more preferably an 0.8mm mesh, even more preferably a 0.5mm mesh and most preferably a 0.4mm mesh, again wherein the meshes are selected from the DIN 4188 mesh series. The solubility of the particle is preferably at least 1g per 100ml at 25°C, more preferably at least 5g, even more preferably at least 8g and most preferably at least 15g per 100ml at 25°C. Finally it is preferred that the particulate material has a hardness of greater than 1, preferably greater than 2 on the Mohs hardness scale. The particle size, solubility and hardness properties confer a crunchy texture to the confectionery itself. Such particles can be present as solid forms of one of the oral care actives outlined above, in the case where the oral care active is a solid, or can be a further particle such as sugar crystals, dried fruits, nuts, etc. The crunchy texture can be used to reinforce the oral care benefits to the consumer. Different crunchy textures can be obtained by milling the particles to the desired size or by blending different commercial grades of particles to achieve the desired crunch. It is preferred the that crunchy sensation remains consumer noticeable for at least 1 minute 30 seconds, preferably for at least 2 minutes and more preferably for at least 2 minutes 30 seconds. However it is also preferred that the crunchy texture has disappeared by 5 minutes, preferably by 4 minutes so that the material does not abrade the dentin or so that the product does not have a gritty residue.

Furthermore the confectionery compositions of the present invention can also be coated. The outer coating may be hard or crunchy. Typically, the outer coating will essentially consist of sorbitol, maltitol, xylitol, isomalt, and other crystallisable polyols. Furthermore the coating will typically consist of several opaque layers, such that the confectionery core is not visible through the coating itself, which can optionally be covered with a

further one or more transparent layers for aesthetic, textural and protective purposes. The outer coating may also contain small amounts of water and gum arabic. A polyol coating can be further coated with wax. The coating is applied in a conventional manner by successive applications of a coating solution, with drying in between each coat, as described in WO99/44436. As the coating dries it usually becomes opaque and is usually white, though other colorants may be added. A polyol coating can be further coated with wax. The coating can further comprise coloured flakes or speckles. If the composition comprises a coat it is possible that one or more of the oral care actives can be dispersed throughout the coat. This is especially preferred if one or more oral care active is incompatible in a single phase composition with another of the actives.

**Balance of the Composition**

Compositions of the present invention preferably comprise safe and effective levels of one or more additional components. Such materials are well known and are readily chosen by one skilled in the art based on the oral care, physical and aesthetic properties desired for the compositions being prepared. Examples of such materials include, but are not limited to fats, solvents, waxes, emulsifiers, softeners, bulking agents, cationic material, buffers, whitening agents, alkali metal bicarbonate salts, thickening materials, humectants, water, surfactants, titanium dioxide, flavouring agents, colouring agents, and mixtures thereof. Those ingredients most commonly used are described in more detail below.

***Abrasive Polishing Materials***

An abrasive polishing material may also be included in the oral compositions. The abrasive polishing material can be any material which does not abrade dentin Typical materials include silica gels and precipitates, aluminas, phosphates, and mixtures thereof. Specific examples include dicalcium orthophosphate dihydrate, calcium pyrophosphate, tricalcium phosphate, hydrated alumina, beta calcium pyrophosphate, calcium carbonate, and resinous abrasive materials such as particulate condensation products of urea and

formaldehyde and others such as disclosed by Cooley et al. in US Patent 3,070,510 issued December 25 1962. Mixtures of abrasives may also be used.

The silica abrasive polishing materials herein generally have an average particle size ranging between about 0.1 to about 30 microns; and preferably froma bout 5 to about 15 microns. The abrasive can be precipitated silica or silica gels such as the silica xerogels described in Pade et al US Patent 3,538,230 issued March 2 1970 and DiGuilio US Patent 3,862,307 issued January 21 1975. Preferred are the silica xeropgels marketed under the name "Syloid" by the W. R> Grace and Company, Davison Chemical Division,. Also preferred are the precipitated silica materials such as those marketed by the J. M. Huber Corporation under the trade name "Zeodent", particularly the silica carrying the designation "Zeodent 119". The types of silica dental abrasives useful in the compositions of the present invention are described in more details in Wason US Patent 4,340,583 issued July 29, 1982. The abrasive in the compositions herein is generally present at a level of from about 6% to about 70%, preferably from about 10% to about 50%, by weight of the composition.

***Surfactants***

The present invention may also comprise surfactants, also commonly referred to as sudsing agents. Suitable surfactants are those which are reasonably stable and foam throughout a wide pH range. The surfactant may be anionic, amphoteric, zwitterionic, cationic, or mixtures thereof. Anionic surfactants useful herein include the water soluble salts of alkyl sulphates having from about 8 to about 20 carbon atoms in the alkyl radical (eg sodium alkyl sulphate) and the water soluble salts of sulphonates monoglycerides of fatty acids having from about 8 to about 20 carbon atoms. Sodium lauryl sulphate and socium coconut monoglyceride sulphonates are examples of anionic surfactants of this type. Many suitable anionic surfactants are disclosed by Agricola et al US Patent 3,959,458 issued May 25 1976. Nonionic surfactants which can be used in the compositions of the present invention can be broadly designed as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkyl-aromatic in nature. The

amphoteric surfactants useful in the present invention can be broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight chain or branched and wherein one of the aliphatic substituents contains froma bout 8 to about 18 carbon atons and one contains an anionic water solubilising group eg carboxylate, sulphonate, suphate, phosphate or phosphonate. Many of these suitable non-ionic and amphoteric surfactants are disclosed by Gieske et al US Patent 4,051,234 issued September 27 1977. The present composition comprises one or more surfactants each at a level of from about 0.25% to about 12%, preferably from about 0.5% to about 8% and more preferably from about 1% to about 6%, by weight of the composition.

***Antioxidants***

Antioxidants are generally recognised as useful in compositions such as those of the present invention. Antioxidants are disclosed in texts such as Cadenas and Packer, The Handbook of Antioxidants, © 1996 by Marel Dekker, Inc. Antioxidants that may be included in the oral care compositions of the present invention include, but are not limited to, Vitamin E, ascorbic acid, Uric acid, carotenoids, Vitamin A, flavenoids and polyphenols, herbal antioxidants, melatonin, aminoindoles, lipoic acids and mixtures thereof.

***Teeth Colour Modifying Substances***

Teeth colour modifying substances may be considered among the oral care actives useful in the present invention. These substance are suitable for modifying the colour of the teeth to satisfy the consumer such as those listed in the CTFA Cosmetic Ingredient Handbook, 3rd Edition, Cosmetic and Fragrances Association Inc., Washington DC (1982), incorporated herein by reference. Specific examples include talc, mica, magnesium carbonate, calcium carbonate, magnesium silicate, aluminium magnesium carbonate, silica, titanium dioxide, zinc oxide, red iron oxide, brown iron oxide, yellow iron oxide, black iron oxide, ferric ammonium ferrocyanide, manganese violet, ultramarine, nylon powder, polyethylene powder, methacrylate powder, polystyrene

powder, silk powder, crystalline cellulose, starch, titanated mica, iron oxide titanated mica, bismuth oxychloride, and mixtures thereof. Typical pigment levels from about 0.05% to about 20%, preferably from about 0.1% to about 15% and most preferably from about 0.25% to about 10%, by weight, of the composition.

Compositions for use herein may also comprise materials that remove or bleach intrinsic or extrinsic stains on or in tooth surfaces. Such substance are selected from the group consisting of the peroxides, metal chlorites, perborates, percarbonates, peroxyacids, persulphates, and combinations thereof. Suitable peroxide compounds include hydrogen peroxide, urea peroxide, calcium peroxide, carbamide peroxide and mixtures thereof. Suitable metal chlorites include calcium chlorite, barium chlorite, magnesium chlorite, lithium chlorite, sodium chlorite and potassium chlorite. Additional bleaching substances may be hypochlorite, and chlorine dioxide. A preferred percarbonate is sodium percarbonate. Preferred persulphates are oxones. The level of these substances is dependent on the available oxygen or chlorine. This level is generally used in compositions of the present invention at levels from about 0.1% to about 35%, preferably from about 1% to about 25% and most preferably from about 5% to about 10%, by weight of the composition.

***Nutrients***

Nutrients may improve the condition of the oral cavity and can be included in the oral care compositions or substances of the present invention. Nutrients include minerals, vitamins, oral nutritional supplements, enteral nutritional supplements, herbal supplements, natural extracts and mixtures thereof as disclosed in Drug Facts and Comparisons (loose leaf drug information service), Wolters Kluer Company, St Louis, Mo., ©1997. Minerals that can be included with the compositions of the present invention include calcium, phosphorus, fluoride, zinc, manganese, potassium and mixtures thereof. Vitamins can be included with minerals or used separately. Vitamins include Vitamins C and D, thiamine, riboflavin, calcium pantothenate, niacin, folic acid, nicotinamide, pyridoxine, cyanocobalamin, para-aminobenzoic acid, bioflavonoids, and

mixtures thereof. Fish oil contains large amounts of Omega-3 (N-3) polyunsaturated fatty acids, eicosapentaenoic acid and docosahexaenoic acid.

***Sweeteners***

Two main types of sweeteners exist; bulk sweeteners and high intensity sweeteners. In general, the amount of sweetener used will vary depending on the sweetener and the overall desired aesthetics but levels used should be high enough such that the desired level of sweetness is achieved independent from the flavour. When bulk sweeteners are used they can also assume the role of the bulking agent or filler within the composition.

Bulk Cariogenic Sweetener: Compositions of the present invention may comprise sweetener materials. Such materials include monosaccharides, disaccharides, polysaccharides and mixtures thereof. Examples include xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, sugar maltose, fructo oligo saccharide syrups, partially hydrolysed starch, or corn syrup solids and mixtures thereof. However, such materials can often lead to the formation of cavities since they are readily metabolised by bacteria and other micro-organisms in the oral cavity. It is preferred that compositions of the present invention comprise less than about 10%, preferably less than about 5%, more preferably less than about 2%, even more preferably less than about 1%, and most preferably less than about 0.5%, by weight of the composition, of cariogenic sweetener. Compositions of the present invention may comprise 0% cariogenic sweetener if desired.

Bulk Non Cariogenic Sweeteners: Compositions of the present invention preferably comprise a non-cariogenic sweetener. As used herein the term "non-cariogenic" refers to sweeteners which are not able to be metabolised by oral microbes and therefore do not contribute to the formation of dental caries. It is preferred that compositions of the present invention comprise greater than about 10%, preferably greater than about 20%, more preferably greater than about 30% and most preferably greater than about 40%, by weight of the composition, of non cariogenic sweetener. Compositions of the present invention may comprise up to 99%, by weight of the composition, of non-cariogenic sweetener if desired.

Preferred bulk non cariogenic sweetening agents are sugar alcohols such as sorbitol, xylitol, mannitol, maltitol, isomalt, hydrogenated starch hydrolisate, insulin, and other non-carigenic edible polyols such as glycerin and erythritol and mixtures thereof. Most preferred are non cariogenic sweeteners selected from the group consisting of maltitol, mannitol, xylitol, sorbitol, sucralose, aspartame and its salts, and mixtures thereof. In general compositions comprise from about 10% to about 80%, more preferably from about 30% to about 70%, by weight, of bulk sweetener.

High Intensity Sweeteners: High intensity sweeteners are preferred over bulk sweeteners for use in compositions of the present invention because, for among other reasons, high intensity sweeteners may prolong the flavour of the finished gum composition during chewing. Suitable high intensity sweeteners include: dipeptide based sweeteners such as L-aspartyl-L-phenylalanine methyl ester (Aspartame) and equivalents (described in U.S. Pat. No. 3,492,131), L-α-aspartyl-N-(2,2,4,4-tetramethyl-3-thietanyl)-D-alaninamide hydrate (Alitame) and the like; saccharin and its soluble salts eg sodium or calcium saccharin salts; cyclamate salts for example acesulfame-K and the like; chlorinated derivatives of sucrose such as chlorodeoxysucrose and the like; and protein based sweeteners, such as Thaumatin (talin). Compositions of the present invention preferably comprise from about 0.01% to about 2.0%, more preferably from about 0.05% to about 0.5%, by weight, of high intensity sweetener.

***Humectants***

The compositions of the present invention may comprise humectants which can serve to prevent the composition hardening upon exposure to air. In addition certain humectants can also act as sweeteners. Suitable humectants include glycerin, sorbitol, polyethylene glycol, propylene glycol and other edible polyhydric alcohols. The humectant is generally present in an amount of from about 0.5% to about 70%, preferably from about 15% to about 55%, by weight of the composition.

***Bulking Agents***

Bulking agents, such as fillers, can also be employed in confectionery. Suitable fillers and bulking agents are generally non-abrasive, preferably with an average particle size less than 5 μm, more preferably less than 3 μm and especially less than 1 μm. Illustrative bulking agents include calcium carbonate or ground limestone, talc, aluminium hydroxide, alumina, aluminium silicates, dicalcium phosphate and mixtures thereof. Compositions preferably comprise up to about 50%, more preferably up to about 30%, and most preferably up to about 10%, by weight, of bulking agent.

***Thickeners***

The present invention provides for compositions in a wide variety of product forms. Typically these compositions comprise some thickening material or binders to ensure that the final composition has the desired consistency. Preferred thickening agents are carboxyvinyl polymers, carrageenan, hydroxyethyl cellulose, and water soluble salts of cellulose ethers such as sodium carboxymethylcellulose and sodium hydroxyethyl cellulose. Natural gums such as gum karaya, xanthum gum, gum arabic, and gum tragacanth can be used as part of the thickening agent to further improve the texture. Thickening agents can be used in an amount of from about 0.1% to about 15%, by weight of the composition.

***Alkali Metal Bicarbonates***

The present invention may also include an alkali metal bicarbonate salt. Alkali metal bicarbonate salts are soluble in water and unless stabilised ten to release carbon dioxide into aqueous systems, although the salt can also function as a buffering agent. Sodium bicarbonate is the preferred alkali metal bicarbonate. The compositions of the present invention comprise from about 0.5% to about 50%, preferably from about 0.5% to about 30%, more preferably from about 2% to about 20% and most preferably from about 5% to about 18%, by weight of the composition.

***Buffering Agents***

The present compositions may comprise a buffering agent. Buffering agents, as used herein, refer to agents that can be used to adjust the pH of the compositions of a range of from about pH 3 to about pH 10. Preferred buffering agents include alkali metal hydroxides, carbonates, sesquicarbonates, borates, silicates, phosphates, imidazole, and mixtures thereof. Specific buffering agents include monosodium phosphate, trisodium phosphate, sodium hydroxide, potassium hydroxide, alkali metal carbonate salts, sodium carbonate, imidazole, pyrophosphate salts, citric acid, and sodium citrate. Buffering agents are used at a level of from about 0.1% to about 30%, preferably from about 1% to about 10% and more preferably from about 1.5% to about 3%, by weight of the composition.

***Additional Chewing Gum Ingredients***

There are several ingredients which are commonly added to chewing gum compositions and which are not commonly used in other types of confectionery. Examples of materials are listed below but this list is not to be considered limiting. Similarly such ingredients can be used in other types of confectionery if desired.

Chewing gum compositions of the present invention may also comprise plasticisers in addition to the resin component. Suitable plasticisers include glyceryl triacetate, acetylated monoglyceride, glyceryl tributyrate, ethyl laurate, ethyl acetoacetate, diethyl tartrate, ethyl or butyl lactates, diethyl malate, ethyl oleate, castor oil, succinylated monoglycerides or mixtures thereof. Glyceryl triacetate and acetylated monoglyceride are preferred. Compositions preferably comprise up to about 10%, preferably from about 0.1% to about 3%, by weight, of plasticiser.

Compositions of the present invention preferably comprise a softener or mixture of softeners which, when incorporated into the gum base, assist in modifying the texture and consistency properties. In particular, they help to soften the chew and to maintain chew softness over an extended period of time.. Suitable softeners include fatty materials such as lanolin, stearic acid, sodium stearate and potassium stearate; polyhydric alcohols such as glycerine, propylene glycol, and the like; and mixtures thereof. Compositions preferably comprise up to about 30%, more preferably from about 0.1% to about 10%, by

weight, of softener. In a preferred embodiment, the chewing gum composition comprises from about 0.1% to about 10%, by weight, of a fatty softener selected from stearic acid, sodium stearate, potassium stearate and mixtures thereof, preferably stearic acid.

The chewing gum compositions preferably comprise an emulsifier such as glycerol monostearate, lecithin, fatty acid monoglycerides, diglycerides, propylene glycol monostearate and mixtures thereof. Compositions comprise up to about 10%, and preferably from about 2% to about 6%, by weight, of emulsifier.

Various fats can also be included in the chewing gum compositions of the present invention. Preferred fats include the hydrogenated vegetable oils such as hydrogenated palm oil, hydrogenated soybean oil, hydrogenated cotton seed oil and various other hydrogenated vegetable oils and mixtures thereof. The fats can suitably be used at a level up to about 20%, preferably from about 1% to about 10%, by weight, of the chewing gum composition.

***Colours***

Colouring agents may also be added to the present composition. The colouring agent may be in the form of an aqueous solution, preferably 1% colouring agent, in a solution of water. Colour solutions generally comprise from about 0.01% to about 5%, by weight f the composition. Opacifiers such titanium dioxide may also be added to the compositions of the present invention generally at a level of from about 0.25% toa botu 5%, by weight of the composition.

***Flavouring Agents***

Compositions of the present invention can preferably comprise a flavouring agent. As used herein the term "flavouring agent" means those flavour essences and equivalent synthetic materials which are added to flavour the composition. The flavouring agent can also include specific materials which are added to provide a warming or cooling sensation.

Flavouring agents are well known in the art. They include synthetic flavours and or oils and or essences derived from plants, roots, beans, nuts, leaves, flowers, fruits and so forth and mixtures thereof. Examples of suitable flavours include lemon, orange, banana, grape, lime, apricot, grapefruit, apple, strawberry, cherry, chocolate, pineapple, coffee, cocoa, cola, peanut, almond, liquorice, cinnamon and the like. The amount of flavouring agent employed is normally a matter of preference but in general they are used in amounts up to about 4%, preferably from about 0.1 to about 1%, by weight of the composition.

Compositions of the present invention can optionally comprise a cooling agent and suitable materials are described in WO 97/06695. Preferred for use herein are physiological cooling agents selected from the group consisting of menthol, peppermint oil, N-substituted –p-menthane-3-carboxamides, acyclic tertiary and secondary carboxamides, 3-l-methoxy propan-1,2-diol and mixtures thereof. Particularly preferred are menthol and menthol containing oils such as peppermint oil. Cooling agents are preferably used at a level of from about 0.001 to about 5%, more preferably from about 0.05% to about 3.5%, by weight of the composition.

Compositions of the present invention can optionally comprise a warming agent. Preferred agents include those selected from the group consisting of vanillyl alcohol n-butyl ether, vanillyl alcohol n-propyl ether, vanillyl alcohol isopropyl ether, vanillyl alcohol isobutyl ether, vanillyl alcohol n-amino ether, vanillyl alcohol isamyl ether, vanillyl alcohol n-hexyl ether, vanillyl alcohol methyl ether, vanillyl alcohol ethyl ether, ginerol, shogaol, paradol, zingerone, capsaicin, dihydrocapsaicin, nodihydrocapsaicin, homocapsaicin, homodihydrocapsaicin, ethanol, isopropyl alcohol, iso-amylalcohol, benzyl alcohol,, chloroform, eugenol, cinnamon oil, cinnamic aldehyde, and mixtures thereof. Warming agents are preferably used at a level of from about 0.001 to about 5%, more preferably from about 0.05% to about 3.5%, by weight of the composition.

**Preparation of Compositions**

The compositions of the present invention are prepared by standard techniques well known to those skilled in the art. If the composition comprises more than one phase, in

general the different phases will be prepared separately, with materials of similar phase partitioning being added in any order. The two phases will then be combined with vigorous stirring to form the multiphase system eg an emulsion or dispersion. Any ingredients in the formulation with high volatility, or which are susceptible to hydrolysis at high temperatures, will usually be added post mixing of the different phases with gentle stirring. If the composition optionally comprises polyphosphate it is preferred that the polyphosphate is not pre-dispersed in water prior to addition to the composition in order to prevent hydrolysis. Typical confectionery methods are highly suitable for manufacturing of compositions of the present invention. Finally if the products are coated confectionery compositions the coating step is conducted as a final step. The coating can be applied by panning or spray dried techniques commonly known to those skilled in the art.

**Method of Use**

According to a second aspect the present invention relates to a method of preventing or treating halitosis comprising applying to the oral cavity a composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* or *Vitis* plant family and mixtures thereof;

(ii) a metal cation selected from the metals of groups 5, 6, 7, 8, 9, 10, 11, 12, 14, 16 of the periodic table and mixtures thereof;

(iii) a pharmaceutically acceptable carrier.

and retaining said composition in the oral cavity for at least 5 seconds, preferably at least 10 seconds, more preferably at least 15 seconds and most preferably at least 30 seconds.

In order to maximise the effects of such methods it is preferred that the compositions of the present invention are formulated such that they remain in the oral cavity for at least 10 seconds. The methods are improved the longer the composition remains in the oral cavity. As such it is preferred that the compositions are formulated to encourage the consumer to retain them in the cavity. Such methods can be reapplied from 1 to about 10, preferably from 1 to about 5 and more preferably from 1 to about 3 times per day. It is

preferred that such methods are used in combination with the usual oral hygiene routine of brushing the teeth at least once or preferably more often per day.

## Examples

The following examples further illustrate the preferred embodiments within the scope of the present invention. These examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention as many variations of the invention are possible without departing from its spirit or scope. Unless otherwise indicated, all ingredients are expressed as a weight percentage of the composition.

### *Chewing gum examples*

| INGREDIENT | I % w/w | II % w/w | III % w/w | IV % w/w | V % w/w | VI % w/w |
|---|---|---|---|---|---|---|
| Sugar | 31.46 | - | - | - | - | - |
| Glucose | 22.00 | - | - | - | - | - |
| Gumbase | 30.00 | 28.00 | 28.00 | 30.00 | 28.00 | 28.00 |
| Sorbitol | - | 38.82 | 41.92 | 37.92 | 35.92 | 32.92 |
| Xylitol | - | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| Isomalt | - | - | - | - | - | - |
| Glycerin | 8.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 |
| Gelatine | - | - | - | - | - | - |
| Water | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Citracidal®* | - | 0.10 | - | - | 3.00 | - |
| Citrus Seed Extract | 1.00 | - | 2.00 | - | - | - |
| Orange Seed Extract | - | - | - | 3.00 | - | 1.00 |
| Sodium polyphosphate | 5.00 | 5.00 | - | 1.00 | 5.00 | 10.00 |
| Flavour | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 |
| Lecithin | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| Acesulfam K | - | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| | | | | | | |
| TOTAL | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| | | | | | | |
| COATING (20 – 30% | | | | | | |

| w/w) | | | | | | |
|---|---|---|---|---|---|---|
| Sorbitol | - | - | - | - | 94.80 | 94.80 |
| Water | - | - | - | - | 2.00 | 2.00 |
| Titanium Dioxide | - | - | - | - | 1.50 | 1.50 |
| Acesulfam K | - | - | - | - | 0.05 | 0.05 |
| Polysorbate 60 | - | - | - | - | 0.15 | 0.15 |
| Flavour | - | - | - | - | 1.50 | 1.50 |
| **TOTAL** | - | - | - | - | 100.00 | 100.00 |

Citricidal ® = Grapefruit seed/pulp extract (Bio/Chem Research; Lakeport, California, USA)

Examples I – VI: Chewing gums: Melt gumbase to 55 - 60°C in sigma blade mixer. Add in bulk sweetener and glycerin, mix. Add in extract and mix. Mix in flavour last . Remove from heat and allow to cool before moulding and cutting. Coating pre-solution is sprayed onto cooled gum in fine layers which are allowed to dry before subsequent layers are added. Sufficient coating is added such that total coating weight is 20 – 30% of final finished pellet weight.

***Non-chewing gum examples***

| INGREDIENT | VII % w/w | VIII % w/w | IX % w/w | X % w/w |
|---|---|---|---|---|
| Sorbitol | - | 93.35 | - | 32.56 |
| Isomalt | 94.84 | - | - | - |
| Glycerin | - | - | 8.00 | 13.00 |
| Gelatine | - | 0.10 | - | - |
| Water | 3.00 | 0.50 | 78.07 | 28.00 |
| Ethanol | - | - | 10.00 | - |
| Precipitated Silica | - | - | - | 20.00 |
| Sodium lauryl sulphate | - | - | - | 2.00 |
| Citracidal®* | - | 0.50 | - | 1.00 |
| Citrus Seed Extract | 1.00 | - | 0.50 | - |
| Eucalyptol | - | - | 0.50 | 0.25 |
| Cetyl pyridinium chloride | 0.10 | - | - | - |
| Sodium polyphosphate | - | 5.00 | - | - |

| | | | | |
|---|---|---|---|---|
| Polethylene glycol | - | - | 1.00 | - |
| Flavour | 1.00 | 1.00 | 1.00 | 1.00 |
| Lecithin | - | - | 0.05 | - |
| Acesulfam K | 0.05 | 0.05 | 0.05 | - |
| Carboxy methyl cellulose | - | - | - | 1.50 |
| Xanthan gum | - | - | - | 0.50 |
| Sodium Fluoride | - | - | - | 0.24 |
| Sodium saccharin | - | - | - | 0.05 |
| Colouring | - | - | 0.02 | |
| Methyl Paraben | - | - | - | 0.07 |
| Propyl paraben | - | - | - | 0.03 |
| | | | | |
| **TOTAL** | 100.00 | 100.00 | 100.00 | 100.00 |

Citricidal ® = Grapefruit seed/pulp extract (Bio/Chem Research; Lakeport, California, USA)

Examples VII: Lozenge. Isomalt is dissolved in water and heated under stirring to 110 - 112 °C and subsequently cooked to 141 - 145°C to boil off water. Batch is drawn down under vacuum and polyphosphate/flavours added at approx 90°C in low humidity environment. Batch is folded on a hot table and subsequently cooled on cold table (20°C) prior to transfer to the batch forming and die cutting apparatus. Final product has a Glass like translucent appearance.

Example VIII: Compressed mint. A pre-formed solution of gelatine and gum products is prepared and sprayed over isomalt to form a granular mixture. This is dried and sieved and subsequently compressed to form tablets.

Example IX: Mouthrinse: Predisperse lecithin and PEG in water and glycerin with sweetener, colour dissolved therein. Disperse flavour in Ethanol and mix into bulk to final rinse.

Example X: Dentifrice: Disperse fluoride, extract and saccharin in water, glycerin and sorbitol solution; mix under vacuum. Blend in silica abrasive with CMC and xanthan dispersed therein. After mixing, add in sodium lauryl sulphate and flavours (with parabens predissolved therein) and mix under vacuum to final product.

**Examples for compositions comprising an extract and a metal cation:**

*Chewing gum examples*

| INGREDIENT | XI % w/w | XII % w/w | XIII % w/w | XIV % w/w | XV % w/w | XVI % w/w |
|---|---|---|---|---|---|---|
| Sugar | 35.57 | - | - | - | - | - |
| Glucose | 22.00 | - | - | - | - | - |
| Gumbase | 30.00 | 28.00 | 32.00 | 30.00 | 30.00 | 30.00 |
| Sorbitol | - | 42.52 | 39.57 | 40.20 | 39.00 | 41.41 |
| Xylitol | - | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| Glycerin | 8.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 |
| Water | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Citricidal ® | 1.00 | 1.00 | 0.10 | 0.50 | 2.00 | - |
| Citrus Seed Extract | - | - | - | - | - | 0.50 |
| Zinc Acetate | 0.40 | 0.40 | - | - | - | - |
| Zinc chloride | - | - | 0.25 | - | 0.20 | - |
| Zinc Citrate | - | - | - | 0.50 | - | - |
| Tin Chloride | - | - | - | - | - | 0.01 |
| Flavour | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 |
| Lecithin | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| Acesulfam K | - | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| | | | | | | |
| **TOTAL** | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| | | | | | | |
| COATING (20 – 30% w/w) | | | | | | |
| Sorbitol | - | - | - | - | 94.80 | - |
| Water | - | - | - | - | 2.00 | - |
| Titanium Dioxide | - | - | - | - | 1.50 | - |
| Acesulfam K | - | - | - | - | 0.05 | - |
| Polysorbate 60 | - | - | - | - | 0.15 | - |
| Flavour | - | - | - | - | 1.50 | - |
| **TOTAL** | - | - | - | - | 100.00 | - |

Examples XI - XVI: Chewing gums: Melt gumbase to 55 - 60°C in sigma blade mixer. Add in bulk sweetener and glycerin, mix. Add in extract and mix. Mix in flavour last .

Remove from heat and allow to cool before moulding and cutting. Coating pre-solution is sprayed onto cooled gum in fine layers which are allowed to dry before subsequent layers are added. Sufficient coating is added such that total coating weight is 20 – 30% of final finished pellet weight.

***Chewing gum examples***

| INGREDIENT | XVII % w/w | XVIII % w/w | XIX % w/w | XX % w/w | XXI % w/w | XXII % w/w |
|---|---|---|---|---|---|---|
| Gumbase | 32.00 | 32.00 | 30.00 | 32.00 | 32.00 | 30.00 |
| Sorbitol | 38.60 | 38.20 | 39.20 | 39.17 | 38.81 | 38.42 |
| Xylitol | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| Glycerin | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 | 5.00 |
| Water | 0.50 | 0.50 | 1.00 | 0.50 | 0.50 | 0.50 |
| Citricidal ® | - | - | - | - | 1.00 | 1.00 |
| Citrus Seed Extract | 0.10 | - | - | - | - | - |
| Orange Seed extract | - | 0.50 | - | - | - | - |
| Lime Seed Extract | - | - | 1.00 | - | - | - |
| Grape Seed extract | - | - | - | 0.50 | - | 0.25 |
| Zinc Acetate | - | 0.50 | 0.50 | | - | 0.25 |
| Zinc chloride | - | - | - | 0.25 | - | - |
| Zinc Citrate | 1.00 | - | - | - | - | - |
| Copper Gluconate | - | - | - | - | 0.01 | - |
| Glass H * | - | - | - | - | - | 2.00 |
| Flavour | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 | 2.50 |
| Lecithin | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| Acesulfam K | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| | | | | | | |
| **TOTAL** | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |
| | | | | | | |
| COATING (20 – 30% w/w) | | | | | | |
| Sorbitol | - | - | - | 94.80 | - | - |
| Water | - | - | - | 2.00 | - | - |
| Titanium | - | - | - | 1.50 | - | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| Dioxide | | | | | | |
| Acesulfam K | - | - | - | 0.05 | - | - |
| Polysorbate 60 | - | - | - | 0.15 | - | - |
| Flavour | - | - | - | 1.50 | - | - |
| | | | | | | |
| **TOTAL** | - | - | - | 100.00 | - | - |

* Glass H (FMC) = Sodium polyphosphate (n = 21). Citricidal ® = Grapefruit seed/pulp extract (Bio/Chem Research; Lakeport, California, USA)

Examples XVII-XXII: Chewing gums: Melt gumbase to 55 - 60°C in sigma blade mixer. Add in bulk sweetener and glycerin, mix. Add in extract and mix. Mix in flavour last . Remove from heat and allow to cool before moulding and cutting. Coating pre-solution is sprayed onto cooled gum in fine layers which are allowed to dry before subsequent layers are added. Sufficient coating is added such that total coating weight is 20 – 30% of final finished pellet weight.

***Non-chewing gum examples***

| **INGREDIENT** | **XXIII % w/w** | **XXIV % w/w** | **XXV % w/w** | **XXVI % w/w** |
|---|---|---|---|---|
| Sorbitol | - | 94.34 | 31.30 | 10.00 |
| Isomalt | 95.00 | - | - | - |
| Glycerin | - | - | 13.00 | 8.00 |
| Gelatine | - | 0.10 | - | - |
| Water | 3.00 | 0.50 | 28.00 | 69.25 |
| Ethanol | - | - | - | 10.00 |
| Precipitated Silica | - | - | 20.00 | - |
| Sodium lauryl sulphate | - | - | 2.00 | - |
| Citracidal®* | 0.50 | - | - | 0.50 |
| Citrus Seed Extract | - | - | 2.00 | - |
| Grape Seed extract | - | 0.50 | - | - |
| Zinc Acetate | 0.45 | - | - | - |
| Zinc chloride | - | - | - | 0.25 |
| Tin Fluoride | - | - | 0.50 | - |
| Tin Chloride/Gluconate | - | 0.01 | - | - |
| Sodium polyphosphate | - | 3.00 | - | - |
| Polethylene glycol | - | - | - | 1.00 |
| Flavour | 1.00 | 1.00 | 1.00 | 1.00 |

| | | | | |
|---|---|---|---|---|
| Acesulfam K | 0.05 | 0.05 | - | - |
| Carboxy methyl cellulose | - | - | 1.50 | - |
| Xanthan gum | - | - | 0.50 | - |
| Sodium saccharin | - | - | 0.05 | - |
| Methyl Paraben | - | - | 0.07 | - |
| Propyl paraben | - | - | 0.03 | - |
| | | | | |
| **TOTAL** | 100.00 | 100.00 | 100.00 | 100.00 |

Example XXIII: Lozenge. Isomalt is dissolved in water and heated under stirring to 110 - 112 °C. Glucose syrup is then added and the mix heated to 141 - 142°C to boil off water. Batch is drawn down under vacuum and polyphosphate/flavours added at approx 90°C in low humidity environment. Batch is folded on a hot table and subsequently cooled on cold table (20°C) prior to transfer to the batch forming and die cutting apparatus. Final product has a Glass like translucent appearance.

Example XXIV: Compressed mint. A pre-formed solution of gelatine and gum products is prepared and sprayed over sugar or dextrose or isomalt to form a granular mixture. This is dried and sieved and subsequently compressed to form tablets.

Example XXV: Dentifrice: Disperse fluoride, extract and saccharin in water, glycerin and sorbitol solution; mix under vacuum. Blend in silica abrasive with CMC and xanthan dispersed therein. After mixing, add in sodium lauryl sulphate and flavours (with parabens predissolved therein) and mix under vacuum to final product.

Example XXVI: Mouthrinse: Predisperse lecithin/ PEG in water and glycerin with sweetener, colour dissolved therein. Disperse flavour in Ethanol and mix into bulk to final rinse.

**WHAT IS CLAIMED IS:**

1. An oral care composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* plant family; the *Vitis* plant family; and mixtures thereof;

(ii) an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; and

(iii) a pharmaceutically acceptable carrier.

2. An oral composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* plant family; the *Vitis* plant family; and mixtures thereof;

(ii) a metal cation selected from the metals of groups 5, 6, 7, 8, 9, 10, 11, 12, 14, 16 of the periodic table and mixtures thereof;

(iii) a pharmaceutically acceptable carrier.

3. A composition according to any of the preceding claims wherein the seed or pulp extract is obtained from the plant group consisting of bergamot; grapefruit; orange; lemon; lime; tangerine; mandarin; satsuma; clementine; citron; shaddock; grape and mixtures thereof; preferably selected from the group consisting of bergamot; grapefruit; orange; lemon; lime; grape; and mixtures thereof, more preferably selected from grapefruit; grape and mixtures thereof.

4. A composition according to any of the preceding claims wherein the extract comprises greater than about 1%, preferably greater than about 5%, more preferably greater than about 10% and most preferably greater than about 15%, by weight of the extract, of polyphenol.

5. A composition according to any of the preceding claims wherein the antibacterial extract comprises less than about 15%, preferably less than about 12% and more preferably less than about 10%, by weight of the extract, of ascorbic acid.

6. A composition according to any of the preceding claims wherein the extract is a seed extract.

7. A composition according to any of the preceding claims wherein the extract is obtained by solvent extraction of the selected material.

8. A composition according to Claim 7 wherein the solvent used for extraction is selected from the group consisting of alcohols, water, acetone, ethyl acetate, glycerol, diethyl ether, propylene glycol or mixtures thereof, preferably the solvent is selected from the group consisting of water, alcohols, glycerol, propylene glycol and mixtures thereof.

9. A composition according to any of the preceding claims wherein the composition comprises from about 0.0001% to about 30%, preferably from about 0.001% to about 15%, more preferably from about 0.01% to about 10%, even more preferably from about 0.1% to about 5% and most preferably from about 0.25% to about 3%, by weight of the composition, of the extract.

10. A composition according to Claim 1 wherein the composition comprises from about 0.01% to about 50%, preferably from about 0.1% to about 15%, more preferably from about 0.25% to about 10%, and even more preferably from about 0.5% to about 7%, by weight, of the oral care active.

11. A composition according to Claim 10 wherein the oral care active is selected from the group of anti-calculus agents comprising polyphosphates, pyrophosphates, phosphonates and mixtures thereof; the group of anti-plaque agents comprising a fluoride ion source, xylitol and mixtures thereof; the group of desensitising agents, preferably potassium nitrate; oral malodour agents preferably zinc or tin salts; and mixtures thereof; preferably the oral care active is an anti-calculus agent; more preferably the oral care active is polyphosphate.

12. A composition according to Claim 11 wherein the polyphosphate material has an average anion chain length of from about 3 to about 40, preferably of from about 6 to about 30; more preferably of from about 10 to about 25 and even more preferably of from about 18 to about 25.

13. A composition according to any of Claims 11 to 12 wherein the polyphosphate is an alkali metal salt, preferably a sodium or potassium salt and more preferably a sodium salt.

14. A composition according to Claim 2 wherein the metal cation is a monovalent or divalent cation selected from the group consisting of zinc, manganese, copper, iron, cobalt, silver, selenium, tin and vanadium; preferably from the group consisting of zinc, manganese, copper, iron, silver, and tin; more preferably from the group consisting of zinc, copper, silver and tin and most preferably from the group consisting of zinc and tin.

15. A composition according to Claim 14 wherein the metal cation is provided as a metal salt selected from the group consisting of acetate, ammonium sulphate, bromide, chloride, chromate, citrate, dithionate, fluorosilicate, tartrate, fluoride, formate, iodide, nitrate, phenol sulphate, salicyclate, sulphate, gluconate, succinate, glycerophosphate, lactate and mixtures thereof; preferred are acetate, bromide, chloride, citrate, dithionate, tartrate, fluoride, formate, iodide, nitrate, sulphate, gluconate, succinate, lactate and mixtures thereof; and more preferred are acetate, chloride, citrate, sulphate, gluconate, succinate, lactate and mixtures thereof.

16. A composition according to any of Claims 14 to 15 wherein the composition comprises greater than 10ppm, preferably greater than 15ppm, more preferably greater than 20ppm, even more preferably greater than 25ppm of the metal cation.

17. A composition according to any of Claims 14 to 16 wherein the composition comprises from about 0.001% to about 5%, preferably from about 0.01% to about 2%, more preferably from about 0.1% to about 1%, even more preferably from about 0.1% to

about 0.5%, by weight of the composition, of metal salt comprising the orally active metal cation.

18. A composition according to any of the preceding claims wherein the composition is a dentifrice, mouthwash, denture cleanser, denture adhesive, confectionery including gum, lozenge and candy, or dental floss.

19. A composition according to any of the preceding claims wherein the composition is a confectionery composition.

20. A composition according to any of the preceding claims wherein the confectionery carrier material is selected from chewing gum base, hard boiled candy base, low boiled candy base, gelatine base, compressed sugar base or mixtures thereof; preferably a chewing gum base.

21. A composition according to Claim 20 wherein the composition comprises greater than about 10%, preferably greater than about 15%, more preferably greater than about 20% and most preferably greater than about 25%, by weight of the composition, of gum base.

22. A composition according to any of the preceding claims wherein the composition comprises less than about 10%, preferably less than about 8%, more preferably less than about 5%, even more preferably less than about 3% and most preferably less than about 2%, by weight of the composition, water.

23. A composition according to any of the preceding claims wherein the composition comprises greater than about 10%, preferably greater than about 20%, more preferably greater than about 30% and most preferably greater than about 40%, by weight of the composition, of non cariogenic sweetener.

24. A composition according to any of the preceding claims wherein the non-cariogenic sweetener is a sugar alcohol, preferably selected from the group consisting of maltitol, mannitol, xylitol, sorbitol, sucralose, aspartame and mixtures thereof.

25. A composition according to any of the preceding claims wherein the confectionery composition has an outer coating.

26. A composition according to any of the preceding claims wherein the oral care active is dispersed throughout the coat.

27. A method of preventing or treating halitosis comprising applying to the oral cavity a composition comprising:

(i) an effective amount of a antibacterial seed or pulp extract from the *Citrus* plant family; the *Vitis* plant family; and mixtures thereof;

(ii) a metal cation selected from the metals of groups 5, 6, 7, 8, 9, 10, 11, 12, 14, 16 of the periodic table and mixtures thereof;

(iii) a pharmaceutically acceptable carrier.

and retaining said composition in the oral cavity for at least 5 seconds, preferably at least 10 seconds, more preferably at least 15 seconds and most preferably at least 30 seconds.

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(54) Title: ORAL CARE COMPOSITIONS

(57) Abstract: An oral care composition comprising:(i) an effective amount of a antibacterial seed or pulp extract from the Citrus plant family; the Vitis plant family; and mixtures thereof;(ii) an oral care active selected from the group consisting of anti-calculus agents; anti-plaque agents; fluoride ion source; desensitising agents; oral malodour control agents; H2 antagonists; and mixtures thereof; and (iii) a pharmaceutically acceptable carrier.The present invention relates to stable oral care compositions, preferably confectionery compositions, which provide enhanced oral malodour benefits combined with one or more additional oral care benefits. The present invention also relates to the use of such compositions to provide a method of treating or preventing oral malodour.

# INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/26

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 20 December 2002 | 03. 01 2003 |

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| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Boeker, R |

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# INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/15268

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/15268

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 27 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 02/15268

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